Vitamin F: 1926–1957

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1926

1. **Boissevain, C.H. “The Action of Unsaturated Fatty Acids on Tubercle Bacilli.”**

Boissevain reports experiments showing the effect of unsaturated fatty acids on the virulence of tubercle bacilli in vitro. (Compare with the work of Larsen on the ricinoleates.) Linoleic and linolenic acids were among the most effective.

—*American Review of Tuberculosis,* Volume 13, pp. 84–89, 1926.

1927

2. **Evans, H.M., and Burr, G.O. “New Dietary Deficiency with Highly Purified Diets.”**

Diets freed from fat but containing adequate amounts of vitamins A, B, D, and E proved incapable of maintaining normal growth and reproduction in animals. The authors conclude that such purified diets demand either an extraordinary and unique amount of some one of the known vitamins or else another and unknown member (F or H) of the vitamin class.

—*Proceedings of the Society of Experimental Biology and Medicine*, Volume 25, pp. 41–48, 1927.

3. **Evans, H.M., and Burr, G.O. “New Dietary Deficiency with Highly Purified Diets: The Biological Effect of Fat in the Diet.”**

Fat improved growth and ovulation in a study of animals fed a fat free diet. When the fats were separated into non-saponifiable matter, glycerol and fatty acids, the improvement was attributed to the fatty acid fraction. The authors considered the favorable substance in fat as representing possibly a new vitamin (F), which, unlike vitamins A, D, and E, is not concentrated in the non-saponifiable fraction.

—*Proceedings of the Society of Experimental Biology and Medicine*, Volume 25, pp. 390–397, 1927.

1928

4. **Evans, H.M., and Lepkovsky, S. “Sparing Action of Fat on the Anti-Neuritic Vitamin.”**

If fat is added to a fat free diet, the amount of anti-neuritic vitamin necessary to establish any definite level of growth or frequency of ovulation is always less than is required when fat is absent. The action of vitamins A, D, and E was excluded, nor was there any anti-neuritic vitamin in the fats themselves. The authors conclude that the action is due to the biological effect of fats previously emphasized by Evans and Burr; therefore, due to vitamin F.

—*Science*, Volume 68, p. 298, 1928.

5. **Archard, C., Grigaut, A., LeBlanc, A., and David, M. “*L’Equilibre Lipoïdique du Sérum Sanguin dans les Maladies Aigües*” (“The Lipoid Equilibrium of the Blood Serum in Acute Diseases”).**

Archard and his associates studied the lipoids of the blood serum, including the iodine number (unsaturated fats) in various diseases. The iodine number is definitely lowered in the acute stage of disease, beginning to rise when convalescence begins and gradually approaching normal as the patient recovers. In fatal cases, the iodine number showed no increase. They concluded that the diminution in the iodine number, or in the unsaturated fats, corresponds with a diminution of the defensive powers of the organism against. invasion. (Compare Boissevain and Larsen.)

—*Journal de Physiologie et de Pathologie Generale*, Volume 26, p. 415, 1928.

1929

6. **McAmis, A.J., Anderson, W.E., Mendel, L.B. “Growth of Rats on Fat Free Diets.”**

During the life of animals grown on fat free diets, the authors noted a poor condition of the fur and bloody urine. Other symptoms suggestive of vitamin deficiency were observed. The authors concluded that, whether the apparent beneficial effects of a small amount of fat is due to its content of vitamin A or other vitamins, or to its action as a vehicle for the fat-soluble vitamins, or whether fat *per se* is essential, had not been conclusively demonstrated by their own experiments.

—*Journal of Biological Chemistry*, Volume 82, p. 247, 1929.

7. **Burr, G.O., and Burr, M.M. “A New Deficiency Disease Produced by the Rigid Exclusion of Fat from the Diet.”**

The first minute description of a fat deficiency syndrome appears in this contribution. Fat deficiency makes for retarded growth, more marked in the male than in the female animal. An abnormal scaly condition of the skin is developed. Hemorrhagic spots appear throughout the entire length of the tail and an actual necrosis results. The hind feet become red and swollen. The hair is filled with dandruff and a tendency for its loss is apparent. Sores appear in the skin, especially the skin of the face. The urinary tract and kidney are extensively involved, and this is undoubtedly an important factor in the death of the animal.

The presence of fatty acids in the diet changed the entire economy of the animals. If the effect be not due to ordinary fatty acids, the authors suggest that a new substance of the nature of an ether soluble organic acid, which could be classed as a vitamin, was responsible for this characteristic dietary deficiency (vitamin F).

—*Journal of Biological Chemistry*, Volume 82, pp. 345–367, 1929.

8. **Evans, H.M., and Lepkovsky, S. “Sparing Action of Fat on the Anti-Neuritic Vitamin (B).”**

The authors refer to their work of 1928, which is amplified in this report. They conclude that, in the absence of anti-neuritic vitamin B, it takes relatively more fat to bring into evidence the sparing action of fat. They defend the view that fats as such undoubtedly exert an important function in the metabolism of the animal other than supplying energy.

—*Journal of Biological Chemistry*, Volume 83, pp. 269–287, 1929.

9. **Brown, J.B. “The Occurrence of a New Highly Unsaturated Fatty Acid in the Lipids of the Brain.”**

Brown reports the finding of unsaturated lipids in beef brain.

—*Journal of Biological Chemistry*, Volume 83, pp. 783–791, 1929.

10. **Brown, J.B., and Rawlins, A.L. “The Effect of Feeding Whale Oil on the Depot Fat of the White Rat.”**

An equilibrium between the food fat and the depot fat was established in between four to six weeks on a given diet. The characteristic wholly unsaturated fatty acids of whale oil were apparently deposited as such.

—*Proceedings of the Society of Experimental Biology and Medicine*, Volume 26, p. 704, 1929.

11. **Taylor, T.C., and Iddles, H.A. “Separation of the Amyloses in Some Common Starches**.”

Cornstarch contained 1.18 percent of fatty material with iodine numbers of from 90.6 to 91.2 in different samples. Investigators using starch in a basic diet in the belief that it is fat free might readily overlook this residuum of highly unsaturated fats, against which error Taylor and Iddles caution.

—*Industrial and Engineering Chemistry*, Volume 18, pp. 713–717, 1929.

1930

12. **Sinclair, R.G. “The Influence of Diet on the Amount and Composition of the Phospholipid Fatty Acids in Various Tissues in the Cat.”**

Sinclair observed that the degree of unsaturation of the fatty acids was definitely higher in the liver, heart, kidney, smooth and skeletal muscles, and intestinal mucosa in cats fed with beef kidney than in cats fed with beef muscle.

—*Journal of Biological Chemistry*, Volume 86, pp. 579–586, 1930.

13. **Burr, G.O., and Burr, M.M. “On the Nature and Role of the Fatty Acids Essential in Nutrition.”**

The most sensitive test of fat deficiency disease is scaliness of the feet. Dandruff is also a reliable indication of the disease. Still greater emphasis is placed on the condition of the kidneys, which are grossly abnormal and show a degeneration, unlike that ascribed to vitamin A deficiency. The kidney disorder due to fat deficiency disease is neither cured nor prevented by increased amounts of the A and D fraction from cod liver oil, but is cured or prevented by the addition of fatty acid not containing vitamin A.

Disturbance of the pituitary is evidenced by the abnormal consumption of water that fat deficient rats display. Vitamin E was without effect in the prevention or cure of the fat deficiency syndrome, nor was regular ovulation induced in female animals by the addition of vitamin E, as was the case with curative oils.

Infertility arising from fat deficiency is not corrected with vitamin E. The fat deficiency syndrome in its entirety was not cured by saturated fatty acids, including stearic, palmitic, myristic, lauric or lower members of the aliphatic series, but it was cured by linoleic acid, either alone or when present in olive oil, lard, corn oil, poppy seed oil, or linseed oil.

The evidence seemed to point to the great effectiveness of linoleic acid, which the authors consider an indispensable essential fatty acid for nutrition. This is the first evidence that suggests the nature of the vitamin F material hinted at in all previous work.

—*Journal of Biological Chemistry*, Volume 86, pp. 587–621, 1930.

14. **Brown, J.B., and Ault, J.C. “Comparison of the Highly Unsaturated Acids of Beef, Hog, and Sheep Brains.”**

A method is described for the isolation of the fatty acids of the brain. This method may become useful for future work on vitamin F.

—*Journal of Biological Chemistry*, Volume 88, pp. 167–174, 1930.

15. **Platonov, G. “The Influence of Unsaturated Fatty Acids on the Virulence of Tubercle Bacilli.”**

Platonov points to recent investigations as having proved the extreme biological importance of lipoids, especially those of the unsaturated fatty acid type. The value of these substances as “nourishment” for the tuberculous patient is thought by Platonov to have been clearly demonstrated during the World War, when the spread of tuberculosis and the peculiar character of the disease at that time furnished proof of diminished resistance brought about by hunger and especially by an insufficiency of fats.

Platonov refers to the work of Goldenberg and Steflso (Russian reference not available), whose determination of the iodine value of various tissues indicated a decrease of the content of unsaturated fatty acid in the organs of the tuberculous and the underfed. Goldenberg and Steflso regard this as the reason for an increased susceptibility for tuberculosis.

Platonov seems to have demonstrated an increased immunity to otherwise lethal doses of tubercle bacilli in guinea pigs by the effect of various oils containing unsaturated fatty acids on tubercle bacilli.

Clinically, the author indicates that his experience is such as to support the conviction that the tubercle bacillus does not easily attack tissues in the human in which unsaturated fatty acids are richly contained. He indicates that the high content of oleins in horse serum and the presence in it of highly unsaturated linoleic acid fits admirably well with the known immunity of the horse to tuberculosis. Platonov indicates that the unsaturated fatty acids should serve as a basis for the dietetic therapy of tuberculosis.

—*American Review of Tuberculosis*, Volume 21, pp. 362–369, 1930.

16. **Mueller, P. “*Ueber die Ungesättigien Fettsäuren Menschlischen Lebers*” (“Unsaturated Fatty Acids of the Human Liver”).**

In human livers, Mueller found that the quantity of unsaturated fatty acids did not increase proportionately with the total fat content of the liver but remained essentially the same for the total liver substance.

—*Archiv fur Experimentelle Pathologie und Pharmakologie*, Volume 147, pp. 219–235, 240, 1930.

17. **Sinclair, R.G. “Some Observations on the Growth of Rats on Fat Free and Fat-Containing Diets.”**

Sinclair reports that rats fed on the fat free diet similar to that used by Burr and Burr developed a scaly condition of the tail without exception and identical with that described by Burr and Burr, if they were kept in cages with a false bottom. The matter of access to feeding on feces is developed.

Cod liver oil did not protect against scaliness of the tail, even when used up to 10 percent by weight of the diet.

—*Proceedings of the Society for Experimental Biology and Medicine*, Volume 27, pp. 1059–1062, 1930.

1931

18. **Graham, C.E., and Griffith. A.H. “Observations on the Nutritive Value of Certain Fats.”**

These investigators corroborated the findings of the Burrs. The scaliness that developed on the feet was not prevented by doubling the yeast intake nor by an active extract of rice polishings, nor by an active liver extract. The condition of the tail was made worse by increasing the cod liver oil. The symptoms were prevented by wheat germ oil, lard or whole liver, wheat germ oil being the most effective and lard the least effective.

Graham and Griffith required additional information before accepting the Burr fat deficiency signs as representing a deficiency in some food factor or as a toxic effect due to the cod liver oil used.

—*Proceedings of the Society of Experimental Biology and Medicine*, Volume 28, pp. 756–761, 1931.

19. **Funk, C., Caspe, S., Caspe. H. “A New Pathological Condition of Probable Dietetic Origin in Rats.”**

These authors report a syndrome analogous to that described by Burr, which they could not prevent by the addition of lard or cod liver oil or linoleic acid to the daily ration. The error in this investigation is discussed subsequently by Burr.

—*Proceedings of the Society for Experimental Biology and Medicine*, Volume 28, pp. 816–818, 1931.

20. **Sueyoshi, Y., and Furokubo, T. “*Ueber die Fettsäuren des Eigelblecithins*” (“On the Unsaturated Fatty Acids in Egg Yolk Lecithin”).**

Egg yolk lecithin was found to contain 73.2 percent of oleic acid, 5.1 percent of clupadonic acid and 2.1 percent of linoleic acid. Previous to this investigation clupadonic acid had been found only in fish oils.

—*Journal of Biochemistry*, Volume 18, pp. 177–183. 1931.

21. **Hume, E.M., and Smith, H.H. “Relation of Fat Free Diet to the Scaly Tail Condition in Rats Described by Burr and Burr.”**

These authors observed the development of the tail condition in rats that received fats in the diet as well as those that did not receive fats. Chick, Roscoe and Aykroyd observe a similar scaly condition in their rats at the Lister Institute, when the animals were housed in cages with coarse wire flooring and diets supplemented by yeast derivatives, rather than whole yeast, as the source of the B vitamins.

—*Biochemical Journal*, Volume 25, pp. 300–306, 1931.

22. **Brown, J.B. “Content and Nature of the Highly Unsaturated Fatty Acids of the Human Brain.”**

Fresh and preserved specimens of human brain showed unsaturated fatty acid content not essentially different from that in the various animal brains examined.

—*Journal of Biological Chemistry*, Volume 92, pp. LXXXVIII–LXXXIX, 1931.

23. **Klenke, E., and v. Schoenebeck, O. “*Uber die hochungesättigien Fettsäuren des Phosphatide aus verschiedenen Organen*” (“Highly Unsaturated Fatty Acids from the Phosphatides in Various Organs”).**

This study corroborates the findings many times elsewhere reported that unsaturated fatty acids occur in phosphatides of many animal organs.

—*Zeitschrift fur Physiologische Chemie*, Volume 154, pp. 191–192, 1931.

24. **Cornbleet, T. “Use of Maize Oil (Unsaturated Fatty Acids in the Treatment of Eczema).”**

Cornbleet notes that over a period of four and a half years a group of eighty-seven patients with chronic eczema responded to treatment with maize oil given by mouth.

The eczema in the cases studied was the condition referred to as allergic eczema, exudative and dietetic eczema, Besnier’s prurigo or generalized neurodermatitis.

All of the patients were over five years of age, most of them adolescents and young adults. All of them had been treated for eczema for several successive years and many since infancy. The use of the oil was not begun until it was established that the patients did not recover easily on any standard therapy.

The first notable improvement was a lightening of the color of the skin. Then the thickened parts became thinner and suppler. Itching was sometimes relieved early. The face was usually the first to improve, the hands and the feet the last.

A few of the patients had asthma, which was improved as well as the eczema. Cornbleet refers to the findings of Burr and of Hansen who describe the action of the oil in eczema as being due probably to its high content of unsaturated fatty acids.

—Archives of Dermatology and Syphilology, Volume 31, pp. 224–226, 1931.

25. **Maronne, P.A. “*Contribution à l’Etude du Metabolisme Normal et Pathologique des Graisses*” (“A Contribution to the Study of the Normal and Pathologic Metabolism of the Fats”).**

Maronne summarizes the experiences of French investigators as having shown that the unsaturated fatty acids are more advantageous to the development of the organism than are the saturated fatty acids. He ascribes the protective function of fats in the subcutaneous tissue to their degree of unsaturation. He points out that, whereas the liver plays an important part in the metabolism and fixation of fats in the organism, recent researches indicate that the lungs, the spleen and the subcutaneous tissue also have a part in this metabolism.

The author opines that obesity is due chiefly to the inability to desaturate the fats assimilated in order that they may be utilized by the organism. He suggests that in the treatment of obesity saturated fats be replaced with unsaturated oils.

—Paris, Thesis.

1932

26. **Gregory, E., and Drummond, J.C. “A Study of Fat Metabolism with Special Reference to Nutrition on Diets Devoid of Fat.”**

These authors report experiments in which a poor condition of the fur and a scaly tail developed on fat free diets. The symptoms were not relieved by the addition of fats containing unsaturated fatty acids but were relieved by the intake of vitamin B.

Their analysis showed that linoleic acid deposited in the adipose tissue of the body is probably derived from the food.

—*Zeitschrift fur Vitaminforschung*, Volume 1, pp. 257–284, 1932.

27. **Hotta, S. “*Die Bedeuiung der Hochungesättigien Fettsäuren in den Organen*” (“The Significance of the Highly Unsaturated Fatty Acids in the Organism”).**

The administration of thyroxin increases the oxidation of the fatty acids in the body, but there is no formation of the highly unsaturated fatty acids.

Less highly unsaturated fatty acids are more easily metabolized than are highly unsaturated fatty acids.

—*Tohoku Journal of Experimental Medicine*, Volume 20, pp. 65–78, 1932.

28. **Roche, A., Roche, J. “*Sur les Accidents Cutanés Attribués à la Carence en Lipide chez le Rat*” (“Cutaneous Eruptions Attributed lo Deficiency of Lipid in the Rat”).**

In two types of diet containing butterfat, rats developed ulceration of the paws and a necrosis of the tail, even when yeast extract was added to the diet, but did not develop these symptoms if fresh yeast was given instead.

—*Comptes Rendus de la Societe Biologique*, Volume 109, pp. 463–464, 1932.

29. **Sinclair, R.G. “The Relationship Between the Amount of Fat Ingested and the Degree of Unsaturation of the Phospholipids and the Neutral Fat in the Tissues of the Rat.”**

Continuing his experiments on the effective fat in the diet, Sinclair suggests that the decline and death of rats on a fat free diet as reported by Burr and Burr may be related to the drop in the degree of unsaturation of the phospholipids below a certain level which is essential for their function.

—*Journal of Biological Chemistry*, Volume 96, pp. 103–125, 1932.

30. **Burr, G.O., Burr, M.M., and Miller, E.S. “On the Fatty Acids Essential in Nutrition.”**

Positive results in the cure of the deficiency disease are marked by renewed growth in weight and length, and by a clearing of the skin and an improvement of the hair coat. Linoleic acid was very effective in curing the deficiency disease as was linolenic acid, both in the form of methyl esters.

Oleic acid was found ineffective. Butter gave negative results. Tung oil had very feeble curative effects.

—*Journal of Biological Chemistry*, Volume 97, pp. 1–9, 1932.

31. **Sinclair, R.G. “Relationship Between Degree of Unsaturation and Composition of Lipids in Animal Tissues.”**

Continuing this type of investigation, Sinclair shows that the amount and kind of fat in the diet exerts a very pronounced and characteristic influence on the degree of unsaturation of both the phospholipids and the neutral fat in the tissues of the body.

—*Journal of Biological Chemistry*, Volume 97, pp. XXXIV–XXXV, 1932.

32. **Eckstein, H.C. “Highly Unsaturated Fatty Acids in Butter.”**

Eckstein demonstrated the presence of acids in butterfat, more highly unsaturated than oleic, his calculation showing about 0.25 percent of linoleic acid.

—*Journal of Biological Chemistry*, Volume 97, pp. XXXV–XXXVI, 1932.

33. **Burr, G.O., and Beber, A.J. “A Study of the Gas Exchange of Rats Suffering from a Deficiency of Unsaturated Fatty Acids.”**

When rats are fat starved but receiving other foods, the respiratory quotient remains above 1.00. When they are completely starved, the quotient drops readily. Rats that have been cured of the fat starved condition show a normal daily metabolic course.

—*Journal of Biological Chemistry*, Volume 97, pp. XXXVI–XXXVII, 1932.

34. **Evans, H.M., and Lepkovsky, S. “Vital Need of the Blood for Certain Unsaturated Fatty Acids.”**

Comparison of the iodine numbers of the various methyl esters employed to correct fat deficiency disease is not a criterion for the content of curative fatty acids. Thus, rats fed a fat free diet have body fats with more unsaturated fatty acids than rats at the time of weaning, yet they possess smaller amounts of the curative unsaturated fatty acids.

—*Journal of Biological Chemistry*, Volume 99, pp. 231–234, 1932.

35. **Evans, H.M., and Lepkovsky, S. “The Sparing Action of Fat on Vitamin B.”**

A study of the sparing effect of various glycerides of oleic acid on vitamin B shows that commercial oleic acids gave decidedly inferior results to the glycerides of purified oleic acid.

—*Journal of Biological Chemistry*, Volume 99, pp. 235–240, 1932.

36. **Berend, N. “*Ueber die Rolle der Stark Ungesättigien Fettsäuren im Organismus*” (“The Role of Highly Unsaturated Fatty Acids in the Organism”).**

In experiments on dogs, fasting produced the reduction in the unsaturated fatty adds of the blood. In pathological lipemia such as occurs in diabetic dogs after the removal of the pancreas, the total fats of the blood are increased, but the unsaturated fatty acids are decreased, so that the percentage of unsaturated fatty acids to total fats is much lower than normal. Large doses of insulin raise this percentage to normal.

—*Biochemische Zeitschrift*, Volume 246, pp. 117–123, 1932.

1933

37. **Hansen, Arild E. “Study of Iodine Number of Serum Fatty Acids in Infantile Eczema.”**

In ten cases of eczema in sixteen normal infants of similar age, the average iodine number of the serum fatty acids in the eczema group was considerably lower than the average iodine number in the control group. This indicates that the serum fatty acids contain less unsaturates in infantile eczema than are present in the blood of normal control infants.

—*Proceedings of the Society for Experimental Biology and Medicine*, Volume 30, pp. 1198–1199, 1933.

38. **Hansen, Arild E., and Burr, G.O. “Studies of Iodine Absorption of Serum in Rats Fed on Fat Free Diets.”**

Because of the apparent necessity for unsaturated fats in the diet, the comparison of the iodine absorption of the serum lipids of control rats with that of animals on fat free diets was studied, and found to be distinct.

The highest value found in fat free animals did not reach the lowest value found in control groups. The results were considered particularly significant since the diet of the controls was comparatively low in fat made up largely from milk.

—*Proceedings of the Society for Experimental Biology and Medicine*, Volume 30, pp. 1200–1201, 1933.

39. **Hansen, A.E. “Serum Lipid Changes and Therapeutic Effects of Various Oils in Infantile Eczema.”**

Oils rich in unsaturated fats gave good clinical results in two infants suffering with severe eczema. Twelve additional cases treated in like manner showed a similar response.

The same diet and the same local care of the skin were observed in all eases. Four cases were studied in respect to the iodine number of the serum fatty acids. The control in this group showed a steady decline, but the cases receiving corn oil and particularly linseed oil showed steady and unquestionably marked gain as the eczema improved.

—*Proceedings of the Society for Experimental Biology and Medicine*, Volume 31, pp. 160–161, 1933.

40. **Burr, G.O., and Brown, W.R. “On the Fatty Acids Essential in Nutrition.”**

In this contribution Burr and Brown review the work of other investigators who reported scaly skin and necrotic tails not associated with fat deficiency and not curable by the administration of suitable fats.

Funk and his associates did not use an adequate amount of vitamin B. The animals of Roche and Roche were so deficient as to have weighed only from 80 to 100 grams after twelve weeks. Hume and Smith admit that the supply of B1 and B2 was insufficient for good growth, nor did their animals always receive sufficient vitamin A as bladder stones developed in some instances. Gregory and Drummond used an inadequate yeast extract, obviously deficient in one or more of the water-soluble vitamins.

The authors fully answer all of the causes for conflict in the partial corroboration of their findings by other investigators. They point out that the fat deficiency disease is characterized by a late failure in growth after an early period of rapid growth in the presence of excess growth factors. The growth failure is accompanied by a high percentage of kidney lesions, abnormal gas exchange and abnormal water consumption.

Whereas necrosis of the tail and scaly skin can result from numerous dietary conditions, it is neither necessary nor justifiable to assume that these diverse causes work through a common factor such as abnormal skin lipids, which they believed responsible for the scaliness in their rats.

—*Proceedings of the Society for Experimental Biology and Medicine*, Volume 30, pp. 1349–1352, 1933.

41. **Rof, J., and Thurnherr, A. *“Ueber das Verhalten der Ungesättigien Fettsäuren bei Experimenteller Nierenschädigung und bei Sauerstoffmangel”* (“The Condition of the Unsaturated Fatty Acids in Experimental Renal Injury and Lack of Oxygen”).**

Poisoning by mercuric chloride showed an increased unsaturated fat content of the kidney, but poisoning by cantharides showed a decrease. The suggestion is made that the difference in effect of the unsaturated fatty acids of the kidney to the two types of renal poisons may be related to the supply and utilization of oxygen. Rats fed on practically fat free diets were found more sensitive to oxygen deprivation than rats fed normal diets, and they also showed a more rapid loss of unsaturated fatty acids in the various organs.

—*Zeitschrift fur die gesamte Experimentelle Medizin*, Volume 88, pp. 693–704, 1933.

42. **Tanze, U. “The Effects of Fatty Acids on Nutrition.”**

Fat-starved rats developed a definite nutritional disorder characterized by a loss of hair, later an inflammation, then dermatitis and scaly skin. The eyes were swollen and closed, though the changes were not due to vitamin A deficiency. There was a retarded growth. Immediately upon restoring linoleic acid to the diet, a soft, fine coating of hair appeared in the denuded areas, growth was normally resumed and the animals became normal. The hair developed a lustrous sheen and the eyes became extremely bright and clear. Oleic acid was ineffective and linolenic acid was neither constant nor at any time as effective as linoleic acid. No sparing action of linoleic acid or linolenic acid for vitamin B was found. Soybean oil was tested but was not comparable with linoleic acid in its effect. The fatty acids from cod liver oil were not effective.

—*Scientific Papers from the Institute for Physical and Chemical Research*, Tokyo, Volume 20, pp. 13–28, 1932; Volume 22, pp. 1–14, 1933.

43. **Hinsberg, K., and Holland, G. *“Ueber das Jodbindungsvermógen im Blute unter Normaler und Pathologischer Verbindung”* (“The Iodine Absorption Value of the Blood Fats in Normal and Pathological Conditions”).**

The values for unsaturated fatty acids are constant for normal persons but are increased in diseases of the liver and in pernicious anemia. The administration of linoleic acid by mouth lowered the blood sugar in diabetics sometimes as much as 100 percent in from three to four hours.

—*Klinische Wochenschrift*, Volume 12, pp. 1601–1602. 1933.

44. **McCollum, E.V., and Becker, J.E. “Linoleic Acid Indispensable to Normal Nutrition.”**

A diet containing everything else which is essential but lacking in linoleic acid will fail to maintain life. It must therefore be provided in food.

—*Food, Nutrition, and Health*, Baltimore, 1933.

1934

45. **Burr, G.O., and Beber, A.G. “Metabolism Studies with Rats Suffering from Fat Deficiency.”**

The experiments clearly show that fat deficient rats are very different from stock animals and that fat deficient rats which have been cured with small doses of fats return to a much more nearly normal gas exchange. The most marked difference shown by fat deficient rats are higher basal rate, higher specific dynamic action of food and higher respiratory quotients. Rats synthesize large amounts of fat daily, but this synthetic fat does not prevent the fat deficiency disease.

—*Proceedings of the Society for Experimental Biology and Medicine*, Volume 31, pp. 911–912, 1934.

46. **Holland, G., and Hinsberg, K. *“Ueber die Physiologische Bedeutung Ungesättigter Fettsäuren und das Jodbindungesvermögen des Blutes*” (“The Physiological Significance of Unsaturated Fatty Acids and the Iodine Absorption of the Blood”).**

The average value of the iodine absorption number of the blood serum is between 500 and 600 mg percent and shows very little variation. In cases with marked cardiac decompensation, the value doubled and dropped to normal as compensation became established. In cardiac disease with good compensation there is little change in the value. In pernicious anemia, liver treatment reduced the iodine absorption value from a high to a normal amount. Upon discontinuing liver treatment, the unsaturated fatty acids again rose.

—*Zeitschrift fur die gesamte Experimentelle Medizin*, Volume 94, pp. 485–494, 1934.

47. **Evans, H.M., Lepkovsky, S., and Murphy, Elizabeth A. “Vital Need of the Body for Certain Unsaturated Fatty Acids (a Digest of Three Communications).”**

A fat free diet, although adequate in other vitamins, showed a failure in the production of young in 20 percent of the female rats after implantation had occurred.

In a much higher percentage, abnormal pregnancies were evidenced by a peculiarly prolonged gestation period and a difficult parturition due to impairment of the birth mechanism. Eighty percent of the young were born dead and the rest died soon after birth. Successful gestation on fat free diets is therefore impossible.

Fortification with carotin or with increased amounts of vitamins A, D and E did not essentially modify the outcome. The addition of a preparation containing essential unsaturated fatty acids improved the percentage of pregnancies, the number of young born alive, the gestation mechanism and period, and the ease of parturition.

The unsaturated fatty acids are again referred to as vitamin F, which, in addition to the early findings of Evans, Lepkovsky and Burr, seems to refer to the identical unsaturates related to the Burr fat deficiency syndrome. Sex instinct is diminished with vitamin F deficiency and restored when vitamin F is returned to the diet.

—*Journal of Biological Chemistry*, Volume 106, pages 431, 441, and 445, 1934.

1935

48. **Oncken, Mildred. “Unsaturated Fatty Acids (Vitamin F) Deficiency.”**

Oncken reviews much of the literature and reports experiments suggesting that the vitamin F content of the blood is reduced even in mild infections such as the common head cold. A deliberate use of vitamin F based on this

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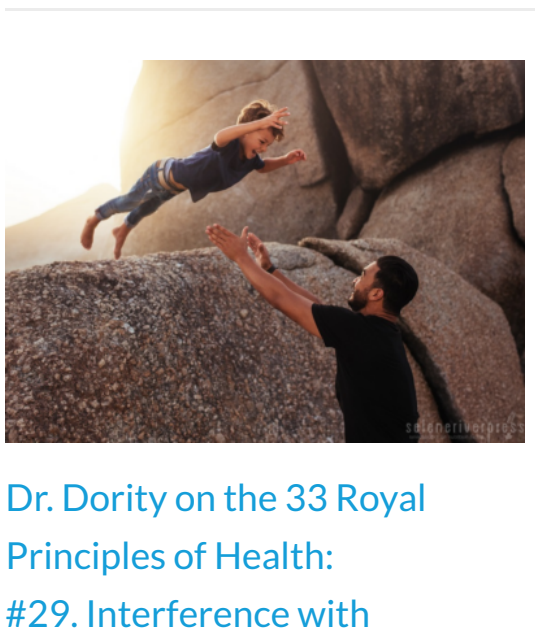

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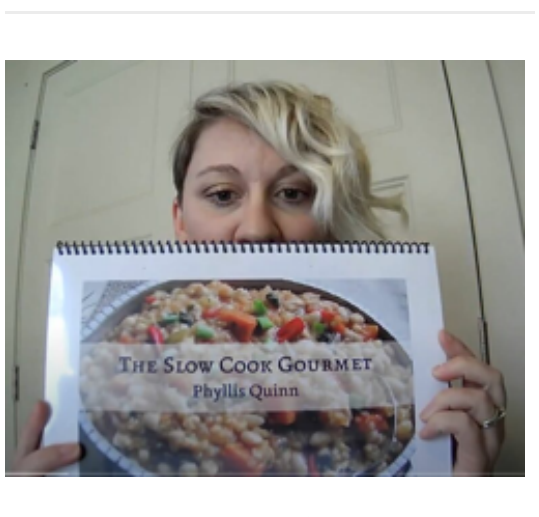

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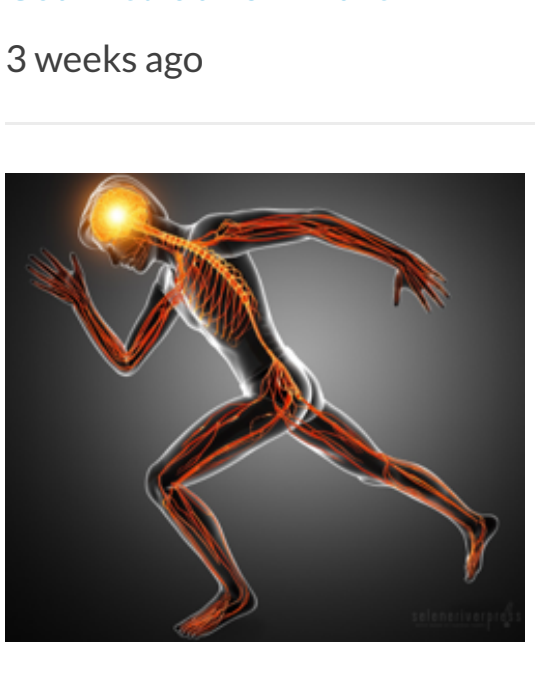

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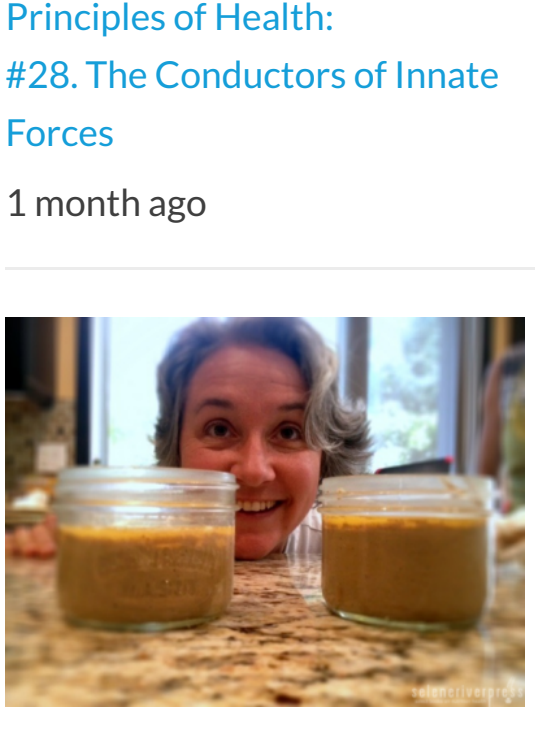

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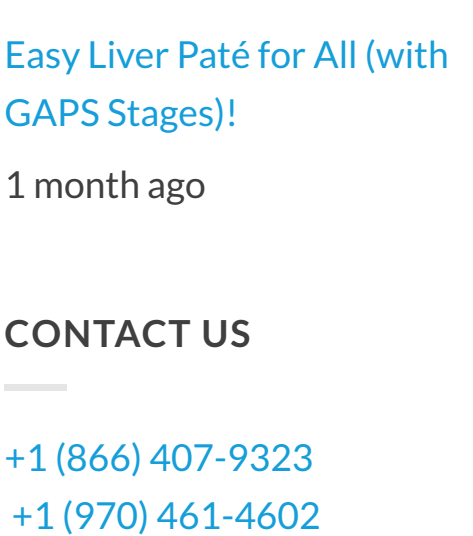

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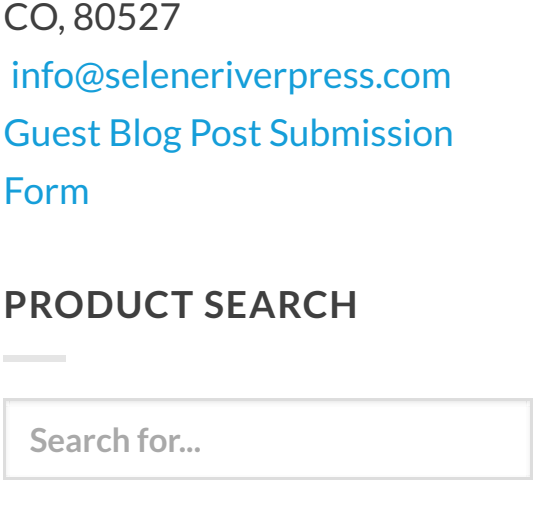

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observation was successful in the treatment of white rats suffering from "snuffles."

Oncken emphasizes the depletion of vitamin F in the daily diet due to the increased use of hydrogenated fats and in many instances of the replacing of fats by nutritionally inadequate substances.

—*Illinois Medical Journal*, Volume 67, pp. 236–239, 1935.

49. **Williams, H.H., and Anderson, W.E. "The Liver and Theory of Fatty Acid Desaturation."**

Reference is made to the indispensability of linoleic acid in the diet and to the probably outstanding importance of this acid in the liver. Linoleic acid is accepted as a necessary constituent of the food together with the amino acids of the proteins the vitamins, salts, etc.

—*Oil and Soap*, March 1935.

50. **Boyd, E.M. "The Lipopenia of Fever."**

Boyd corroborates the finding that the blood lipids respond to febrile conditions. He points out that the onset of fever is accompanied by a sudden flood of unsaturated fatty acids (vitamin F) into the bloodstream. He interprets the result as indicating a general derangement of fat metabolism in fever, which he suggests as being due probably to an excessive removal of transport fats from the plasma by the active body tissues. An excellent bibliography is appended.

—*Canadian Medical Association Journal*, Volume 32, pp. 500–506, 1935.

51. **Haven, Francis L. "Effect of Dietary Fats on Growth and Composition of Tumors."**

In a study of the various fats, it was found that the growth tendencies of rat tumors on coconut oil diets were greater than those of rat tumors on cod liver oil diets.

The inhibitory action of unsaturated fats on the growth of tumors is explained by the theory that phospholipids function as oxygen transport agents within the cells. The incorporation of unsaturated fatty acids into the phospholipids of tumor cells may aid respiration and thus may inhibit tumor growth.

—*Proceedings of the Society for Experimental Biology and Medicine*, Volume 82, pp. 734–737, 1935.

52. **Lepkovsky, S., Ouer, R.A., and Evans, H.M. "The Nutritive Value of the Fatty Acids of Lard and Some of Their Esters."**

Under conditions that were strictly constant so that the only variable factor was the character of the fat employed, lesions corroborating the kidney lesions first suggested by Burr were found. The glycerides of the fatty acids of lard seem to be the best for the prevention of these lesions. Since glycerides are hydrolyzed in the intestinal tract, the authors found it difficult to understand the inferiority due to the direct feeding of a mixture of glycerol and free fatty acids, as compared with the glycerides of the fatty acids themselves.

—*Journal of Biological Chemistry*, Volume 108, pp. 431–438, 1935.

53. **Evans, H.M., and Lepkovsky, S. "The Sparing Action of Fat in Vitamin B."**

The experiments reported here permit the conclusion that fat does not spare vitamin B by reducing the loss of this vitamin in the feces but by decreasing the amount of this vitamin dissipated in the metabolism of the rat. The liver was found to be the site of the greatest initial withdrawal of vitamin B, and a high fat diet definitely diminished the withdrawal.

—*Journal of Biological Chemistry*, Volume 108, pp. 439–455, 1935.

54. **Sinclair, R.G. "Metabolism of the Phospholipids."**

A micro-procedure is described, making it possible to determine the relative proportions and the iodine numbers of the saturated solid and the unsaturated liquid fatty acids in 30 to 40 mg samples of material.

The author finds evidence of the selection and retention of highly unsaturated fatty acids by tissue phospholipids. From previous findings Sinclair suggests that there are at least two classes of phospholipids; one comprises the more highly unsaturated phospholipids and functions in the essential make-up of the cell, and the other comprises less saturated phospholipids functioning as an intermediary product in the metabolism of fat. Both classes are present in the liver but in skeletal muscle the phospholipid is mainly of the nonmetabolic type.

—*Journal of Biological Chemistry*, Volume 111, pages 261, 275, and 515, 1935.

55. **Lecoq, R.** ***"Peut-on, dans une Ration Equilibŕee, Substituer Aux Glycerides Les Acides Gras qui Leur Correspondent"*** **("Question of Substituting Fatty Acids for Glycerides in a Balanced Diet").**

Lecoq reports experiments on pigeons in which it was found that in a balanced diet containing natural fats such as butter, linseed oil, etc., it was impossible to substitute the corresponding fatty acids without causing malnutrition and signs of vitamin B deficiency. The author notes that some essential substance is likely to be removed in the process of preparing the fatty acids.

—*Comptes rendus d l'Academie des Sciences*, Volume 200, pp. 1979–1980, 1935.

1936

56. **Cox, W.M., and Inboden, M. "A Purified Diet Satisfactory for Growth, Reproduction and Lactation in Rats."**

The purified diet suggested consists of casein, dextrin, lard, wheat germ oil, aqueous extract of brewer's yeast, carotene, calcium acetate, salt mixture and rice cellulose.

—*Proceedings of the Society for Experimental Biology and Medicine*, Volume 34, pages 443 and 446, 1936.

57. **Brown, W.R., and Burr, G.O. "Some Recent Studies in Fat Deficiency."**

A composite growth curve for more than 200 rats on fat deficient diets are practically identical with the earlier work published by Burr and his associates. Relatively impure diets can be used for producing fat deficiency symptoms.

Buttermilk lipids, though rich in unsaturates, are not curative when fed to rats showing the fat deficiency syndrome. Yeast oil is also ineffective. Scaliness decreases during the summer months so that humility is related to the severity of the symptoms being less severe in summer and more severe in winter.

—*Journal of Biological Chemistry*, Volume 114, p. XVI, 1936.

58. **McAmis, A.J., and Sweet, M.H. "The Influence of a Diet Rich in Avocado on Growth and on the Quality of Body Fat in the Albino Rat."**

When avocado was used as the main constituent of the diet and supplemented by dried skim milk, the growth of rats compared favorably with that of animals on adequate stock diets.

—*Journal of Biological Chemistry*, Volume 114. p. LXIV, 1936.

59. **Sinclair, R.G. "Evidence of the Synthesis of Essential Unsaturated Fatty Acids by the Rat.**

Sinclair finds that the growth of rats raised on a diet devoid of unsaturated fatty acids is distinctly subnormal, yet considerable. A high intake of elaidin almost completely abolishes the limited synthesis of highly unsaturated fats from carbohydrates and thus prevents growth.

—*Journal of Biological Chemistry*, Volume 114, p. XCIV, 1936.

60. **Stosser, A.V. "Iodine Number of Serum Fatty Acids in Acute Infections of Infants with and Without Eczema."**

Stosser refers to the work of Hansen and to his own previous report, observing that the total cholesterol value was much less at the height of the infection than during the period of convalescence. Pneumonia showed the greatest change; eczema showed some change.

—*Proceedings of the Society for Experimental Biology and Medicine*, Volume 84, pp. 10–11, 1936.

61. **Shepherd, M.I. "Vitamin F in Skin Creams."**

Shepherd reviews the development of the vitamin F concept in relation to the lecithin, cholesterol and vitamin F content of the skin. The empiric use of linseed oil is reviewed in the light of its effectiveness because of its unsuspected vitamin F content. A ratio for normal skin between cholesterol, lecithin and total unsaturates including vitamin F was given as 1:1:3.

—*Drug and Cosmetic Industry*, March 1936.

62. **Shepherd, M.I., and Linn, E.R. "Evaluation of Vitamin F."**

A detailed procedure for the quantitative estimation of vitamin F effectiveness is proposed, suggesting a unit. The vitamin F is externally applied. Vitamin F is present in normal rat skin but not in rat skin derived from animals suffering the Burr fat deficiency syndrome. Emphasis is made on the probable value of the vitamin F content of lard when this material serves as an ointment paste in the treatment of eczema and other conditions.

—*Drug and Cosmetic Industry*, May 1936.

63. **Shepherd, M.I., and McMath, Dorothy C. "Lipid Balance in Creams."**

Creams which represent modified ointments are formulated so as to include the fat ratio in which the lipids comprising lecithin, cholesterol and vitamin F are proportioned in the ratio of 1:1:3.

—*Drug and Cosmetic Industry*, July 1936.

64. **Glennon, Katherine. "Vitamin Soaps."**

The effectiveness of official Sapo mollis and the dependence of this effectiveness on the presence of vitamin F in the linseed oil from which Sapo mollis is prepared, suggests that all soap becomes more effective if a definitely known quantity of vitamin F is purposely added. The quantity suggested is about 125 vitamin F units per gram of soap.

—*Soap*, November 1936.

65. **Pacini, August J., and Avis, H. Wentworth. "Vitamin F in Cosmetics."**

A complete discussion of the natural occurrence of vitamin F is presented. Oils are divided into four groups: the wide variation of vitamin F content due to natural causes is shown for each of the four groups. Vitamin F deficiency symptoms are detailed, and the curative effects of vitamin F on the human skin are exemplified by actual microphotographs.

The relation of vitamin F to the luster and pliability of human hair is disclosed as a corroboration in the human of the improvement in fur quality frequently reported for laboratory animals.

The inadvisability of using other than biologically standardized vitamin F material is compared to the identical case in the use of cod liver oil as in vitamin A and D source without further knowledge of the exact A and D content.

The resemblance of vitamin F to the ricinoleates in a remarkable detoxifying property is discussed.

Some evidence is advanced which indicates that all vitamin F is linoleic acid but not all linoleic acid isomers are vitamin F. Thus, neither the unsaturation of the fat nor the chemical detection of a linoleic isomer is sufficient as a measure of vitamin F effectiveness. Biological assay is imperative.

—*Soap, Perfumery and Cosmetics*, September 1936.

66. **Pacini, August J. "Vitamin F (Unsaturates)."**

Symptoms suggesting vitamin F deficiency are apparently more prevalent among humans than symptoms suggesting deficiencies due to all other vitamins combined. Dry skin, brittle, lusterless and falling hair, dandruff, brittle fingernails and eczema, and kidney disease are exaggeratedly numerous and ubiquitously distributed. The relation of vitamins to perfumes passing through intermediate products such as sex hormones and the like is pointed out as a relation much deeper than the apparent superficial difference. The importance of measured vitamin values and the elimination of the use of crude, unstandardized materials is stressed. The immunological and detoxifying properties of vitamin F, like those of the ricinoleates, are discussed.

—*American Perfumer*, December 1936.

1937

67. **Hansen, A.E. "Serum Lipids in Eczema and in Other Pathological Conditions."**

The values for cholesterol content, total fatty acid content and iodine absorption of the serum were determined for seventy normal subjects and an equal number of patients suffering from a variety of clinical disorders, including eczema. Interest centered chiefly about twenty-three in ants and eight older children with eczema. The great majority of eczematous subjects showed a significant lowering of the iodine number of the fatty acids of the serum when compared with normal subjects of similar ages. This alteration was demonstrated to be independent of such important factors as previous diet and infection. The degree of saturation of the fatty acids of the serum was found to be essentially normal in a series of non-eczematous patients presenting a wide variety of pathologic conditions. A significant rise in the iodine number of the serum lipids of eczematous subjects followed the administration of large doses of oils with high iodine numbers. Coincident with this in many instances was an unmistakable improvement in the clinical condition of the patient. These observations strongly suggest a fundamental relationship between the pathogenesis of eczema and a disturbance in lipid metabolism.

—*Am. J. Dis. Children*, 53, 933, 1937.

68. **Burr, G.O., and Beber, A.J.** made the early observation that fat-deficient rats had an abnormally high metabolic rate.

—*J. Nutrition*, 14, 553, 1937.

69. **"Rats and Vitamin F in Cosmetology."**

Mary Imogene Shepherd, PhD, says that "it is now definitely established that the complete removal of certain indispensable unsaturated fatty acids from the diet results in the appearance of "deficiency" symptoms that involve: 1. the skin and epidermal appendages; 2. the endocrine glands; 3. certain of the viscera, in particular the kidneys; 4. the general state of nutrition; 5. and possibly the constitutional physiology that permits allergic susceptibility to take place."

—Bureau of Investigation, *JAMA*, April 10, p. 1280, 1937.

1938

70. **Turpeinen, O. "Further Studies on the Unsaturated Fatty Acids Essential in Nutrition."**

The effectiveness of substances to cure fat-deficiency disease in rats were tested…

Erucic, ricinoleic 12:13-oleic, and chaulmoogric acids proved ineffective.

In experiments conducted with four levels of linoleic acid, it was found that the maximal growth response in plateaued fat-deficient females ensued when approximately 100 mg of methyl linoleate was fed daily; twice this amount did not further improve growth, whereas half of it was patently inadequate.

Linoleyl alcohol showed some curative properties, although it was less effective than linoleic acid.

Arachidonic acid was found to be a powerful curative agent; it produced maximal growth response when 33 mg of the methyl ester was fed daily and was hence very definitely superior to linoleic acid in this respect.

—*Journal Nutrition*, 15, 351, 1938.

71. **Birch, T.W. "The Relation Between Vitamin B6 and the Unsaturated Fatty Acid Factor."**

Evidence is presented that shows that two factors are concerned in the production and cure of the acrodynia-like dermatitis of rats. One is the water-soluble basic substance vitamin B6; the other is fat-soluble and is present in the fatty acid fraction of maize oil. The evidence indicates that the fat-soluble factor is similar to the "fatty acid factor" of Burr and Burr and to the fat-soluble anti-dermatitis factor of Hogan and Richardson.

It is suggested that the physiological function of vitamin B6 is connected with the utilization of the unsaturated fatty acids.

—*J. Biol. Chem.*, 124, 775, 1938.

72. **Hume, E.M., Nunn, L.C.A., Smedley-MacLean, I., Smith, H.H. "Studies of the Essential Unsaturated Fatty Acids in Relation to the Fat Deficiency Disease of Rats."**

It is concluded that the ability of unsaturated fatty acids to supplement a fat free diet in promoting weight increase is not necessarily associated with ability to heal skin lesions.

—*Biochem. J.*, 32, 2162, 1938.

73. **Nunn, L.C.A., and Smedley-MacLean, I. "The Nature of the Fatty Acids Stored by the Liver in the Fat-Deficient Disease of Rats."**

Linoleic and linolenic acids appear to be the building stones essential for the production of more highly unsaturated acids that play some unknown part in enabling the animal to store fat in its depots and tissues.

—*Biochem. J.*, 32, 2178, 1938.

74. **Brown, W.R., Hansen, A.E., Burr, G.O., McQuarrie, I. "Effects of Prolonged Use of Extremely Low-Fat Diet on an Adult Human Subject."**

It cannot be assumed that the human subject could subsist indefinitely on a diet completely devoid of the unsaturated fatty acids.

—*J. Nutr.*, 16, 511, 1938.

75. **Salmon, W.D. "The Effect of Certain Oils in Alleviating Localized Erythematous Dermatitis (Acrodynia or Vitamin B6 Deficiency in Rats)."**

Rats receiving a fat free diet supplemented with carotene, vitamin D concentrate, thiamine, riboflavin, and a limited amount of aqueous extract from brewers' yeast, which has been subjected to dry heat treatment (24 hours at 120–130°F) before extraction develop a severe form of erythematous dermatitis. The further addition of corn oil, linseed oil, wheat germ oil, or the fatty acids of linseed or soy bean oil, cures or prevents the dermatitis. If the heated yeast extract is omitted, however, the oils do not cure or prevent the condition.

It appears that the effective oils do not contain the entire dermatitis-preventing factor but may contain an essential part of the factor that supplements the heated yeast extract.

Methyl esters of linoleic or linolenic acid are less effective than the oils or their total fatty acids in curative tests but do delay onset of symptoms in preventive tests. Cod liver oil or coconut oil has little activity. Nicotinic acid alone or in combination with other supplements has no effect on the course of the disease.

—*J. Biol. Chem.* 123, civ., 1938.

1939

76. **Martin, G.J. "Studies of Fat-Free Diets."**

Data are presented comparing the average maximum growth of rats on fat-free diets with that of rats fed methyl linoleate curatively and prophylactically. The minimum level of methyl linoleate for optimal growth effects has been tentatively placed at or below 1 drop (30 mg) per day per rat. The inability of methyl linolenate to supplement methyl linoleate is proved.

The observation has been made that rats fed a highly purified synthetic diet, complete in all known dietary essentials, plateau at subnormal weights. These rats show positive growth response to supplements of brain and liver.

—*J. Nutrition* 17, 127, 1939.

77. **Quackenbush, F.W., Plarz, B.R., Steenbock, H. "Rat Acrodynia and the Essential Fatty Acids."**

Complete healing of acute or chronic acrodynia in rats, obtained by administration of peanut oil or wheat oil. Aeration or ultraviolet did not destroy the activity in peanut oil.

Cures were produced with ½ drop of wheat germ oil, corn oil or Wesson oil, 10 drops of coconut oil or 25 drops of butterfat. Lesions not prevented or cured with hydrogenated coconut oil.

—*J. Nutrition* 17, 115, 1939.

78. **Sperry, Warren M. "The Relation of Vitamins to the Metabolism of Neutral Fat."**

McHenry and Gavin showed that thiamine, riboflavin, and rice polish concentrate have associated effects upon the amount of body fat, which in the presence of these substances was increased in rats disproportionately to the food intake.

Birch showed that both unsaturated fatty acid and vitamin B6 are concerned in the cure of acrodynia-like dermatitis of rats and suggested that the function of B6 is related to the utilization of unsaturated fatty acids.

—*Annual Review of Biochemistry*, 8:231–248, (237), 1939.

1940

79. **Hevesy, G.C., and Smedley-MacLean. "The Synthesis of Phospholipin in Rats Fed on the Fat-Deficient Diet."**

The turnover of P in the muscle phospholipin in the rats receiving only the fat-free diet is about one-third more active than in either of the groups which have received the supplements of unsaturated acids. This result is of particular interest since the evidence from the investigation of the R.Q. of rats with fat-deficiency disease suggested that more fat was being burnt than in the normal rat. Thus Wesson & Burr (1931) showed that in such rats in the first hours following carbohydrate feeding, the R.Q. is well above l, indicating formation of fat from carbohydrate and that rats in the early stages of the disease show assimilatory and basal metabolic rates 25 percent greater than normal. This result was confirmed by Burr & Beber (1937), who found a much higher metabolic rate for the fat-starved rats. They state that for 12 to 16 hours a day the R.Q. of fat-starved rats remained above 1, but when the rats stopped eating the R.Q. dropped rapidly, indicating the burning of much fat.

Since in the experiments described by Smedley-MacLean and Nunn (1940) the proportions of fatty acids in the liver, kidney and muscle tissues of the rats suffering from fat deficiency showed no diminution, it could be inferred that the formation of fatty acid from carbohydrate and its conversion into phospholipin proceeded normally. The results of the radioactive injections show that in animals almost devoid of the higher unsaturated acids there is no diminution in the turnover of P in the liver and kidneys and presumably therefore phospholipin is being synthesized as actively in the rat suffering from long-standing fat deficiency as in those with the more normal diet containing the essential unsaturated acids.

—*Biochem. J.*, 34, 903, 1940.

80. **Russell, W.C., Taylor, M.W., and Polskim, L.J. "Fat Requirements of the Growing Chick."**

1. The extensive removal of substances soluble in diethyl ether from an ordinary poultry growing mash did not retard growth of chicks significantly up to 14 weeks of age, when care was taken to provide the vitamins removed by the extraction process.
2. Although dietary fat was reduced to a very low level (0.1%) or less), crystalline carotene was utilized. However, the quantity of carotene fed was several times the minimum requirement.
3. The depot fat formed on the low-fat ration was more saturated than that of chicks on the normal ration. On the other hand, the liver fat of both groups showed essentially the same degree of saturation. The liver fat was less saturated than the depot fat.

—*J. Nutrition*, 19, 555, 1940.

81. **Sinclair, R.G. "Growth of Rats on High-Fat and Low-Fat Diets Deficient in the Essential Unsaturated Fatty Acids."**

On a diet of casein, salt mixture, dried yeast and the fat, elaidin, supplemented with vitamins A and D, rats cease growing when only about 100 gm in weight. After several weeks at constant weight they go into a decline and die. Since growth and health are readily restored by feeding a little corn oil, the impairment in growth is attributed to a severe deficiency of the essential unsaturated fatty acids.

Replacement of the elaidin by sucrose also results in a rapid and extensive gain in weight. A similar, though smaller, gain occurs when the elaidin diet is replaced by one rich in carbohydrate and very poor in fat.

It is concluded that the better growth of rats on a high carbohydrate than on a high fat diet, both equally poor in essential fatty acids, is due, in part at least, to the synthesis of the fatty acids necessary for growth. An increase in the requirement of essential fatty acids by rats on a high fat diet may also contribute to the poor growth obtained.

—*J. Nutrition*, 19, 131, 1940.

82. **Burr, G.O., Brown, J.B., Kass, J.P., Lundberg, W.O. "Comparative Curative Values of Unsaturated Fatty Acids in Fat Deficiency."**

Unsaturated fatty acids (linoleic, linolenic, arachidonic and cod liver oil acids) show differences in growth and skin effects. They should no longer be treated as an interchangeable group but should be used individually in nutrition studies.

—*Proc. Soc. Exp. Biol. Med.*, 44, 242, 1940.

83. **Schneider, H.A. "Butterfat in Dermatitis-Producing Diets."**

The anti-dermatitis action of fresh butter fat has been confirmed.

Destruction of the anti-dermatitis potency of butterfat has been demonstrated in a diet in which the butterfat was allowed to become rancid.

—*Proc. Soc. Exp. Biol. Med.*, 44, 266, 1940.

84. **Richardson, L.R., and Hogan, A.G. "Relation of Pantothenic Acid to Dermatitis of the Rat."**

Birch reported that two factors are required to prevent or cure acrodynia. One is vitamin B6 the other is one of the essential unsaturated fatty acids.

—*Proc. Soc. Exp. Biol. Med.*, 44, 583, 1940.

85. **Burr, G.O., Brown, J.B., Kass, J.P., Lundberg, W.O. "Comparative Curative Values of Unsaturated Fatty Acids in Fat Deficiency."**

Schneider, Ascham, Plarz and Steenbock recently summarized their findings on the anti-acrodynic potency of foods. Their table shows that cod liver oil is very poor and the linolenic acid of linseed oil is ineffective. Those oils highest in linoleic acid are most effective (corn oil and wheat germ oil). Salmon recently reported that methyl linoleate was much more effective than methyl linoleate in curing the skin of B6 deficient rats,

Unsaturated fatty acids (linoleic, linolenic, arachidonic and cod liver oil acids) show differences in growth and skin effects.

—*Proc. Soc. Exp. Biol. Med.*, 44, 242, 1940.

86. **Hoagland, R., and Snider, G.G. "Nutritive Properties of Certain Animal and Vegetable Fats."**

Thus, Hoagland and Snider observed greater gains in weight in rats on diets containing 30 or 55 percent of lard than in one having 5 percent of this fat.

—*U.S. Dept. Agric. Tech. Bull.*, No. 725, 1–12, 1940.

87. **Hume, E.M., Nunn, L.C.A., Medley-MacLean, I., and Smith, H.H. "The Relative Curative Potencies of Methyl Linoleate and Methyl Arachidonate, with a Note on the Action of the Methyl Esters of Fatty Acids from Cod Liver Oil."**

1. Methyl arachidonate was prepared from pig's liver and from ox suprarenal glands.
2. The material was tested curatively on rats receiving the fat-free diet of Burr et al. in simultaneous comparisons with methyl linoleate.
3. In confirmation of the work of Turpeinen, methyl arachidonate was found to be more active than methyl linoleate in promoting weight increase; its activity in curing skin lesions was, however, no greater than that of methyl linoleate,
4. Methyl arachidonate, like methyl linoleate, unless given in very small doses, continued to exercise a beneficial effect for some time after dosage had been suspended.
5. Methyl esters of cod liver oil fatty acids were given prophylactically to young rats on the fat-free diet. The activity in promoting weight increase and in giving protection against skin lesions was very slight.

—*Biochem. J.*, 34, 879, 1940.

1941

88. **MacKay, E.M., and R.H. Barnes. "Cure of Signs of Egg White Disease by Corn Oil Fatty Acids and Vitamin B6."**

Summary: Egg white injury or acrodynia in the albino rat, which occurs when commercial dried egg white is included in the diet of this animal in a substantial amount, develops much more slowly if 10 percent of the fat in the diet is in the form of corn oil instead of Crisco. If vitamin B6 is injected into corn oil fed rats, the signs and symptoms of the egg white acrodynia almost entirely disappear.

—*Proc. Soc. Exp. Biol. Med.*, 46, 353, 1941.

89. **Smedley-MacLean, I., and Hume, E.M. "The Storage of Fat in the Fat-Starved Rat."**

Excerpt: The conclusion was drawn that a plentiful supply of highly unsaturated acid was necessary for the formation of new tissue but not for the maintenance of the normal metabolism of the cell.

—*Biochem. J.*, 35, 990, 1941.

90. **Sherman, W.C. "The Effect of Certain Fats and Unsaturated Fatty Acids upon the Utilization of Carotene."**

Various natural oils were fed to vitamin A-deficient rats receiving controlled levels of carotene. Of the oils tested, soybean oil gave the best growth. Cottonseed oil, linseed oil, corn oil, and wheat germ oil also had a beneficial effect upon the growth. Butterfat and coconut oil had no appreciable effect.

—*J. Nutr.*, 22, 153, 1941.

91. **Salmon, W.D. "The Relation of Pantothenic Acid, Pyridoxine and Linoleic Acid to the Cure of Rat Acrodynia."**

It is thus apparent that three factors are necessary for complete cure of rat acrodynia. These are pyridoxine, linoleic acid, and pantothenic acid.

—*Journal Biol. Chem.*, 140, CIX, 1941.

92. **Kelsey, F.E., and Longenecker, H.E. "Distribution and Characterization of Beef Plasma Fatty Acids."**

The major portion of plasma linoleic acid is combined with cholesterol.

—*J. Biol. Chem.*, 139, 727–740, 1941.

1942

93. **Quackenbush, F.W., Kummerow, F.A., and Steenbock, H. "The Effectiveness of Linoleic Arachidonic, and Linolenic Acids in Reproduction and Lactation."**

Quantity of nutrients required for reproduction was about twice that necessary for the cure of the dermal lesions produced by a fat-free diet. Linolenic acid was recorded as being ineffective in allowing a normal reproduction while linoleic and arachidonic acids were recorded as having about the same biopotency in furnishing needs for pregnancy.

—*J. Nutrition,* 24, 213–224, 1942.

94. **Gullickson, T.W., Fountaine, F.C., and Fitch, J.B.**

Feeding tests were conducted to compare the feeding value of the following fats and oils for calves: butterfat, lard, tallow, coconut oil, peanut oil, corn oil, cottonseed oil and soybean oil. The effect of a very fat-poor diet on calves was also determined. Each oil or fat was added to skim milk, homogenized to form a product containing 3.5 percent fat and fed along with a low-fat content concentrate mixture, cod liver oil and some alfalfa hay. One control group was fed normal whole milk not homogenized. Test periods ranged from a few days to about six months.

In average daily gain in weight as well as in general well-being, the calves fed butterfat excelled those in all other groups. Following closely were those receiving lard and tallow. Corn oil, cottonseed oil and soybean oil were the least satisfactory. The average daily gains of calves in the latter three groups were: .40 pounds, .31 pounds, and .32 pounds, respectively. They appeared unthrifty, listless and emaciated. Some calves in these groups died and others were saved only by changing to whole milk.

Post-mortem examinations showed considerably more fat deposited in calves fed butterfat than in those that had been fed other oils and fats.

—*J. Dairy Sci.*, 25, 117, 1942.

95. **Burr, B.O. "Significance of the Essential Fatty Acids."**

The unsaturated acids function primarily as essential building stones in cell structures and in mobile lipids. It would not be surprising to find numerous ill effects on domestic livestock and man of the present trend toward high carbohydrate diets containing small amounts of highly saturated fats.

It will be recalled that kidneys and other organs of all fat deficient rats also show changes, it seems likely that many tissues will eventually be found to show adverse effects of vitamin deficiencies in animals eating limited amounts of linoleic acid.

—*Feder. Proc.*, 1, 224, 1942.

96. **Quackenbush, F.W., Kummerow, F.A., and Steenbock, H. "The Effectiveness of Linoleic, Arachidonic, and Linolenic Acids in Reproduction and Lactation."**

1. On a low-fat diet furnishing only 3.0 mg. of unsaturated lipid or a calculated maximum of 0.8 mg of linoleic acid per rat per day, rats were raised to maturity and bred. After a prolonged gestation period and severe hemorrhage in parturition, the young were born dead or died soon after birth. A scaly condition of the hind paws and tail was observed after about 10 weeks on the diet.
2. Ethyl linoleate and ethyl arachidonate prevented or cured the dermal symptoms completely and produced normal young which were weaned at the age of 3 weeks with an average body weight of 40 gm. The requirement for these acids appears to be higher than previously estimated.
3. Ethyl linolenate did not make possible the production of normal young; neither did it cure the dermal

symptoms.

4. Fat analyses revealed a remarkable constancy in both the percentage of total fat and the iodine values of the fat, irrespective of the dietary supplements.

—*J. Nutrition*, 24, 213, 1942.

97. **Richardson, L.R., Hogan, A.G., and Itschner, K.F. "Vitamin B6 Pantothenic Acid, and Unsaturated Fat Acids as They Affect Dermatitis in Rats."**

It is believed that the unsaturated fatty acids do not replace pyridoxine but simply delay the onset of the skin symptoms.

—*Univ. Missouri Agric. Expt. Sta. Research Bull.*, No. 333, 3–12, 1941; *Chem. Abst.*, 36, 2591–2592, 1942.

1943

98. **Dr. Grollman & Harrison. "Fish Oils May Be Source of Blood Pressure Remedy."**

Fish body and liver oils contain a substance that is effective in reducing high blood pressure in rats.

—*Science News Letter*, May 1, 1943.

1944

99. **Loosli, J.K., Lingenfelter, J.F., Thomas, J.W., and Maynard, L.A. "The Role of Dietary Fat and Linoleic Acid in the Lactation of the Rat."**

Linoleate acid not proved to be an essential factor in case of the rat; however, corn oil did produce a stimulatory effect and hydrogenated coconut oil was ineffective.

—*J. Nutrition*, 28, 81–88, 1944.

1946

100. **Hansen, Arild E., MD, PhD, and Burr, Geo. O., PhD. "Essential Fatty Acids and Human Nutrition."**

Hansen and Burr of the University of Texas School of Medicine believe that the unsaturated fatty acids may be concerned with the natural integrity of the skin, and clinical experience with 120 patients with an intractable form of eczema suggests that supplements of fats or oils rich in the essential fatty acids may be highly useful in preventing and correcting the disease.

—*J. Am. Assoc.*, 132, 855–9, 1946.

101. **Forbes, E.B., Swift, R.W., James, W.H., Bratzler, J.W., and Black, A. "Further Experiments on the Relation of Fat to Economy of Food Utilization: 1. By the Growing Albino Rat."**
—*J. Nutrition*, 32, 387–396, 1946.

Forbes, E.B., Swift, R.W., Thacker, E.J., Smith, V.F., and French, C.E. "Further Experiments on the Relation of Fat to Economy of Food Utilization: 2. By the Mature Albino Rat."
—*J. Nutrition*, 32, 397–403, 1946.

Information from above two articles. (It was subsequently recorded by Forbes and coworkers that the increasing efficiency of the high-fat diets was related to a decrease in total heat production.)

1947

102. **Scheer, B.T., Soule, D.F., Fields, M., and Deuel, H.J. Jr. "The Effect of Fat Level of the Diet on General Nutrition: 11. Growth, Mortality, and Recovery in Weanling Rats Maintained on Restricted Calories."**

In tests in which rats were fed diets for 12 weeks after weaning so restricted in calories that growth did not take place, sexual maturity did not obtain, irrespective of the level of fat in the diet. However, when the rats were allowed to consume the several diets ad libitum, sex maturity was observed in the following average periods: 0% fat (14.7 days); 5% fat (11.9 days); 10% fat (10.5 days); 20% fat (7.7 days); and 40% fat (9.8 days).

—*J. Nutrition*, 33, 583–592, 1947.

103. **Scheer, B.T., Dorst, S., Codie, J.F., and Soule, D. "Physical Capacity of Rats in Relation to Energy and Fat Content of the Diet."**

Using a swimming test devised by Scheer as a method for providing exhausting exercise, it was found that the average duration over which rats could swim could be considerably extended if they had been receiving high-fat diets.

—*Am. J. Physiol.*, 149, 194–203, 1947.

104. **The Netherlands Letter: "New Vitamin in Butter."**

During investigations at the University of Amsterdam, C.B. Jensen and J. Boer found that summer butter showed a more favorable influence on the growth of young rats than other fats, even winter butterfat…The factor responsible for this better growth apparently is an unsaturated fatty acid, because the growth-promoting action of summer butterfat and of the fatty acids from summer butterfat disappears on hydrogenation.

—*J.A.M.A.*, 133:1299, 1947.

105. **Scheer, B.T., Soule, D.F., Fields, M., and Deuel, H.A. Jr. "The Effect of Fat Level of the Diet on General Nutrition: 11. Growth, Mortality, and Recovery in Weanling Rats Maintained on Restricted Calories."**

In the case of weanling rats, which had been stunted by caloric restriction for 12 weeks, Scheer and collaborators found that when the depleted rats were fed ad libitum on diets containing 0, 5, 10, 20, or 40% of fat, the groups receiving the three highest levels of fat did equally well and were far better than the other groups. However, the highest potential for growth still remaining after 12 weeks of ad libitum feeding was found in the group receiving the 40% fat diet; by this time, practically no gain in weight was being obtained by the rats on 0% or 5% fat diets.

—*J. Nutrition*, 33, 583–592, 1947.

106. **Stoesser, A.V. "Influence of Soybean Products on the Iodine Number of the Plasma Lipids and the Course of Eczema."**

Hansen observed that the degree of unsaturation of the fatty acids in the blood as measured by the level of iodine absorption was lower than normal, not only Burr's rats suffering from fat deficiency but also in infants with eczema. The ingestion of raw linseed oil, corn oil, and lard revealed that fats with a relatively high unsaturated fatty acid content could raise the iodine absorption values of the plasma lipids of these young children…

Infants with more severe skin changes had iodine numbers averaging 71, which is much below normal. After three or more weeks of ingestion of the soybean milk, the values rose until an average of 118 was reached, which is within the normal range. This situation was associated with favorable response to external therapy…

Some observations presented in previous communication in which it was noted that during acute infections of the respiratory tract in infants with eczema, the skin showed temporary improvement at the onset of fever, but was much worse thereafter. This may be due to the fact that early in an acute infection there is a sudden flood of unsaturated fatty acids into the bloodstream to be followed by a fall to abnormally low levels.

—*J. Allergy*, 18, 29, 1947.

1950

107. **Doctors Mead and Decker. "Fatty Acids May Be Important to Health."**

The beneficial effect of essential fatty acids may be important for good health as vitamins.

Experiments with young mice showed that animals on a fatty acid-deficient diet never attain normal growth and manifest certain skin diseases like those resulting from a lack of vitamins. In addition, female mice become sterile and adults succumb quickly to radiation.

—*Science News Letter*, June 3, 1950.

108. **Deuel, Harry James Jr. (1897), Samuel Mendel Greenberg (1915), Clarence Edward Calbert (1913), Evelyn Elizabeth Salvage (1924), and Tomoko Fukui (1924). "The Effect of Fat Level of the Diet on General Nutrition: V. The Relationship of the Linoleic Acid Requirement to Optimum Fat Level."**

The injection of the growth hormone did not result in growth for the fat-deficient rats.

Cottonseed oil added to diet for rats showed better results in regards to acceleration in growth than linoleate.

—*J. Nutrition*, Vol. 40, No. 3, March 1950.

109. **Rogers, C.S., Ferguson, C.C., Friedgood, C.E., and Vars, H.M. "Influence of Fat in the Diet Upon Nitrogen Balance and Liver Regeneration."**

Moderately high-fat diets served as effectively in permitting the regeneration of liver tissue as did low-fat diets.

—*Am. J. Physiol.*, 163, 347–353, 1950.

110. **Greenberg, S.M., and Deugel, H.J. Jr. "The Protective Effect of High-Fat Diets on Immature Rats Fed Thyroid."**

Greenberg and Deuel reported that the presence of cottonseed oil in the diet not only permitted normal growth when thyroid powder was given but likewise prevented mortality.

—*Journal Nutrition*, 42, 279–284, 1950.

1951

111. **Holman, R.T. "Metabolism of Isomers of Linoleic and Linolenic Acids (18399)."**

From these experiments it is apparent that trans-isomers of the "essential" fatty acids are converted to inactive forms of polyunsaturated acids, which are, however, detectable spectrophotometrically. Conversely, the detection of polyunsaturated acid in a tissue does not imply that these substances are biologically active. However, this factor is not likely to affect studies of animals fed natural diets.

—*Proc. Soc. Exptl. Biol. and Med.* 76, 100–2, 1951.

1952

112. **Witten, R.W., and Holman, R.T. "Polyethenoid Fatty Acid Metabolism: VI. Effect of Pyridoxine on Essential Fatty Acid Conversions."**

Young rats were placed on a fat-deficient, pyridoxine deficient diet, and when definite symptoms of acrodynia appeared after 4 weeks, supplementary diets were given.

Pyridoxine plus linoleate relieved symptoms and stimulated growth, fat synthesis, and arachidonate synthesis much more than either supplement alone. Pyridoxine plus linolenate stimulated growth, fat synthesis and hexenoic acid synthesis much more than did either supplement alone, but dermal symptoms were not relieved.

The metabolic products of linoleate and linolenate formed under the influence of pyridoxine stimulate synthesis of fat. These products may be arachidonate and hexaenoate, respectively.

—*Arch. Biochem. and Biophys.*, 41, 266–73, 1952.

113. **Kummerow, F.A., Pan, H.P., and Hickman, H.**

Female rats which had grown to maturity on a fat-free diet and bred, gave birth to young which were born dead or died soon after birth. When this diet was supplemented with 5% hydrogenated fat, the animals gave birth to living young which did not live more than 72 hours, while those fed 5% com oil weaned 85% of their young.

Total fat analyses of representative female rats and their newly born young indicated that the animals which had been kept on the fat-free diet were deficient in arachidonic acid and not deficient in fat *per se*. The largest differences occurred in the phospholipid fraction of the fat extracted from the young. The phospholipids of the young from animals which had received corn oil contained from 5 to 10, and those from animals on hydrogenated fat, two times more arachidonic acid than those from rats on the fat-free diet.

—*J. Nutrition*, 46, 489–98, 1952.

114. **Greenberg, S.M. "The Protective Effect of Dietary Fat on Immature Rats Fed Thyroid."**

In later tests, Greenberg was able to point out a protective action against thyroid exhibited independently by linoleic acid and by cottonseed oil.

—*J. Nutrition*, 47, 31–39, 1952.

1953

115. **Prof. Humberto Aviles. "Discovery of the Anti-Cancerous Properties of the 'F' Vitamine (Reptiline)."**

Summary:

1. It has been confirmed that Reptilina (Anticancerous factor from Reptiles, Aviles H. Professor, Bol. No. 1 Dec. 52) is vitamin F made by the fatty acids; linoleic, and arachidonic. They relieve the pain in 5 minutes and they are carcinolitics.
2. It has been discovered that vitamin F relieves the nausea and vomiting of pregnancy and chronic abortion.
3. It has been confirmed that vitamin F neutralizes the effects of atomic radiation.
4. The theory has been confirmed that cancer is due to a lack of vitamin F (hypovitaminosis F).
5. The theory has been developed that cancer is a hybrid that has its origin in the colibacilo, paracolibacilo) of constipation, and it has been proved statistically that this paracolibacilo is present in 99% of the people suffering from cancer.

—*Biochem. of Cancer Dept.*, Angela Peralta No. 30, Guadalajara. Jal. Mex. Aug. 1, 1953.

116. **Kramar, J., and Kovacs, J. "The Influence of Animal and Vegetable Fats Upon the Capillaries in Relation to Exudative Diathesis."**

Presented at the Annual Meeting of the Hungarian Pediatric Society, Budapest (June 1939), cited by Kramar, J., and Levine, V.E.J.

As early as 1939, Kramar and Kovacs made the first clinical observations that the resistance of the skin capillaries in human subjects, especially in those with allergic manifestation, was higher on a dietary regimen containing vegetable fat than on one composed entirely of fats of animal origin.

—*Nutrition*, 50, 149–160, 1953.

117. **Carver, D.S. and Johnson, E.L. "Unidentified Growth Factors for the Chick in Vegetable Oils and Fatty Concentrates."**

Crude oil, wheat germ oil, oleic acid and linoleic acid either alone or combined, added to a basal ration caused an increase in growth in chicks. Oleic acid and wheat germ oil were the most potent.

—*Poultry Sci.* (Dept. Poultry Husb., Iowa State Coll., Ames) 32, 701–705, 1953; M.J. Head, *Nut. Abstrs. & Reviews*, Vol. 24, p. 240, 1954.

118. **Kinsell, L.W., Michaels, G.D., Partridge, J.W., Boling, L.A., Balch, H.E., and Cochrane, G.C. "Effect Upon Serum Cholesterol and Phospholipids of Diets Containing Large Amounts of Vegetable Fats."**

Reports that blood cholesterol level of patients having high cholesterol values as a result of diabetes or related conditions can be lowered by the administration of vegetable fats but not by that of animal fats; it is possible that this effect in man may be associated with the effect of the essential fatty acid content of the fats.

—*J. Clin. Nutrition*, 1, 224–231, 1953.

119. **Hansen, A.E., Holmes, S.G., and Wiese, H.F. "Fat in the Diet in Relation to Nutrition of the Dog: IV. Histologic Features of Skin from Animals Fed Diets with and Without Fat."**

Lack of fat in diet brings about definite changes in both epidermis and dermis; also, hair follicles, sebaceous glands and capillaries are all affected.

—*Chem. Abst.*, 47, 9447–9448, 1953.

1954

120. **Deuel, H.J. Jr., Martin, C.E., and Alfin-Slater, R.B. "The Effect of Fat Level of the Diet on General Nutrition: XII. The Requirement of Essential Fatty Acids for Pregnancy and Lactation."**

The lowest mortality rate and highest weaning weights of rats were obtained when the nursing mothers received 100 or 200 mg of cottonseed oil daily or 80 mg of linoleate. Results showed that a certain definite level of essential fatty acids is required for satisfactory lactation as well as for successful pregnancy.

—*J. Nutrition*, 54, 193–199, 1954.

121. **Alfin-Slater, R.B., Aftergood, L., Wells, A.F., and Deuel, H.J. Jr. "The Effect of Essential Fatty Acid Deficiency on the Distribution of Endogenous Cholesterol in the Plasma and Liver of the Rat."**

It has been demonstrated that on a fat-free diet the level of liver cholesterol becomes elevated in rats concomitantly with a decrease in level of plasma cholesterol.

—*Arch. Biochem. Biophys.*, 52, 180–185, 1954.

122. **Deuel, Harry James Jr., Charlotte Roe Martin, Roslyn Berniece Alfin-Slater. "The Effect of Fat Level of the Diet on General Nutrition: XII. The Requirement of Essential Fatty Acid for Pregnancy and Lactation."**

Essential fatty acids required in diet of female rat to insure survival of pups after birth.

—*J. Nutrition*, Vol. 54, No. 2, October 1954.

123. **Cheng, A.L.S., Alfin-Slater, R.B., and Deuel, H.J. Jr. "The Effect of Fat Level of the Diet on General Nutrition: XIII. The Effect of Increasing Doses of X-Irradiation on the Protective Action of Fat on Radiation Injury."**

Rats having had X-irradiation survived longer upon being given cottonseed oil…Protective effect of fat against X-ray occurs under variety of conditions related to intensity of dose and to frequency.

—*J. Nutrition*, 54, 201–207, 1954.

124. **Kinsell, L.W. "Effects of High-Fat Diets on Serum Lipids."**

Blood cholesterol of patients with a high cholesterol from having had diabetes or related conditions is lowered by taking vegetable fats not animal fat. It is probable the effect may be associated with effect of essential fatty acid content in fats.

—*J. Am. Dieter. Assoc.*, 30, 685–688, 1954.

1955

125. **Peifer, J.J., Holman, Ralph T. "Essential Fatty Acids, Diabetes, and Cholesterol."**

One approach reported briefly here, relates essential fatty acids, diabetes, and cholesterol.

Because of the accelerated mobilization and catabolism of fats associated with diabetes, it seemed that the diabetic animal might deplete its EFA reserves faster…

The results support the assumption that the diabetic rat is more rapidly depleted of his EFA…Dietary cholesterol does not significantly influence the development of the deficiency in the diabetic animal…

EFA deficiency in the diabetic animal and EFA deficiency intensified by dietary cholesterol in the nondiabetic animal is similar…

Because of the evident relationships of cholesterol and diabetes to atherosclerosis, it might be suggested that atherosclerosis is an expression of EFA deficiency or its faulty metabolism.

—*Archives of Biochemistry and Biophysics*, 57, p. 520, 1955.

1956

126. **"Unsaturated Fatty Acids and Serum Cholesterol Levels."**

That large concentrations of unsaturated vegetable oils included in formula feeding result in a decrease of serum cholesterol in a majority of individuals seems established.

—*Nutrition Reviews*, Vol. 14, No. 11, pp. 327–328, 1956.

127. **Schroeder, Henry A., MD. "A Practical Method for the Reduction of Plasma Cholesterol in Man."**

A practical method has been devised to lower plasma cholesterol in ambulatory patients, based on a diet fairly low in saturated fatty acids but providing an adequate intake of linolenic acid, a metal chelator, and pyridoxine. Plasma levels fell variably but considerably in most of 20 patients.

—*Journal of Chronic Diseases*, Vol. 4, No.5, p.461, November 1956.

1957

128. **American Medical Association's Council on Foods and Nutrition, Dr. W. Stanley Hartcroft. "Fats, Cholesterol, and Atherosclerosis."**

Excerpt: Emphasis on effect of corn oil and certain other fats containing unsaturated fatty acids that reduce blood cholesterol levels…

Suggestion of approach to some problems of diet.

1. Reduce total fat intake with a proportionate increase of unsaturated fats, keeping in mind the caloric value of all the foods.

—*J.A.M.A.*, April 20, p. 1486, 1957.

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